

15 liver cDNA libraries with a nucleic acid probe corresponding approximately to the 5' 0.5 kb of the fohd013a05m MRP- β insert. This probe was prepared by isolating an approximately 0.5 kb SacI fragment from fohd013a05m. The cDNA sequence presented in SEQ ID No: 1 comprises the sequence of the fohd013a05m MRP- β insert and the sequence of an additional 66 upstream (5') nucleotides. The open reading frame (ORF) of the SEQ ID No: 1 cDNA encodes an MRP- β polypeptide (SEQ ID No: 2) 1437 amino acid residues in length and in addition, includes a 0.42 kb 3' untranslated region. The ORF start site indicated in SEQ ID No: 1 (at nucleotides 116-118 of SEQ ID No: 1) is the first in-frame ATG codon downstream from the TGA stop codon at nucleotides 23-25 of SEQ ID No: 1.

In the Claims:

Please cancel claims 116, 119 and 134.

Please amend claims 106-108, 115, 117-118, 120-129, and 131-133, as follows:

106. (Twice Amended) A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell with a candidate modulator of MRP- β ;
- (b) assaying the level of expression of the MRP- β nucleic acid molecule set forth as SEQ ID No: 1 in said cell, wherein a detectable fluctuation in said level indicates that said candidate modulator is an MRP- β modulator.

107. (Twice Amended) A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell with a substrate exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide, the amino acid sequence of which shares at least 75% sequence identity with SEQ ID No: 2, as determined by the ALIGN algorithm (weight residue table = PAM120, gap length penalty = 12, gap penalty = 4);
- (b) contacting said cell with a candidate modulator of MRP- β ;

- (c) assaying for a detectable fluctuation in export or sequestration of said substrate, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

108. (Twice Amended) A method of identifying a modulator of MRP- β , comprising the steps of:

- D6
- (a) contacting a cell with a cytotoxin exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide, the amino acid sequence of which shares at least 75% sequence identity with SEQ ID No: 2, as determined by the ALIGN algorithm (weight residue table = PAM120, gap length penalty = 12, gap penalty = 4);
- (b) contacting said cell with a candidate modulator of MRP- β ;
- (c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.
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115. (Amended) The method of claim 107 or 108, wherein the amino acid sequence of the vector-derived MRP- β polypeptide shares at least 85% sequence identity with the amino acid sequence of SEQ ID No: 2.

D8

117. (Amended) The method of any one of claims 107 and 138-140, wherein the substrate is a cytotoxin.

118. (Amended) The method of any one of claims 107-108 and 138-143, wherein MRP- β expression confers a survival advantage on said cell

120. (Amended) The method of any one of claims 107-108 and 138-143, wherein the cell expresses a cell surface MRP- β polypeptide.

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121. (Amended) The method of any one of claims 106-108 and 138-143, wherein the cell is a eukaryotic cell.

122. (Amended) The method of any one of claims 106-108 and 138-143, wherein the cell is a yeast or mammalian cell.

123. (Amended) The method of any one of claims 106-108 and 138-143, wherein the cell is a human cell.
124. (Amended) The method of any one of claims 106-108 and 138-143, wherein the cell is a MCF-7 cell.
125. (Amended) The method of claim 106, wherein assaying the level of MRP- β comprises assaying the amount or rate of production of MRP- β nucleic acid molecule.
- D9 126. (Amended) The method of claim 106, wherein assaying the level of MRP- β comprises assaying the amount or rate of production of MRP- β polypeptide is said cell.
127. (Amended) The method of claim 106 or 135, wherein a detectable decrease or cessation of MRP- β expression indicates that the candidate is an inhibitory modulator.
128. (Amended) The method of claim 106 or 135, wherein a detectable increase in MRP- β expression indicates that the candidate is a stimulatory modulator.
129. (Amended) The method of any one of claims 106-108 and 138-143, wherein the candidate modulator is contacted with the cell prior to, concomitantly with, or following exposure to the substrate.
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131. (Amended) The method of claim 108, wherein a detectable decrease in survival indicates that the candidate is an inhibitory modulator.
- D10 132. (Amended) The method of any one of claims 106-108, wherein the candidate modulator is selected from the group consisting of a natural metabolite, a synthetic chemical, a synthetic metabolite, a toxin, an antibiotics, an element of a combinatorial chemistry library, an element of a nucleotide library, an element of a peptide library, a naturally sourced chemical, a naturally sourced cell secretion product, a cell lysate,
133. (Amended) The method of any one of claims 106-108, wherein the candidate modulator is a small molecule.
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Please add new claims 135-143, as follows:

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135. (New) A method of identifying a modulator of MRP- β , comprising the steps of:
- (a) contacting a cell with a candidate modulator;
 - (b) assaying the level of expression of the MRP- β polypeptide set forth as SEQ ID No: 2 in said cell, wherein a detectable fluctuation in said level indicates that said candidate modulator is an MRP- β modulator.
136. (New) The method of claim 107 or 108, wherein the amino acid sequence of the vector-derived MRP- β polypeptide shares at least 95% sequence identity with the amino acid sequence of SEQ ID No: 2.
137. (New) The method of claim 107 or 108, wherein the amino acid sequence of the vector-derived MRP- β polypeptide comprises the amino acid sequence of SEQ ID No: 2.
138. (New) A method of identifying a modulator of MRP- β , comprising the steps of:
- (a) contacting a cell with a substrate exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide encoded by a nucleic acid molecule which hybridizes under conditions of hybridization in 0.5M NaHPO₄ at 65°C followed by washing in 0.1xSSC at 68°C to a complement of the nucleic acid molecule having the sequence of SEQ ID No: 1;
 - (b) contacting said cell with a candidate modulator of MRP- β ;
 - (c) assaying for a detectable fluctuation in export or sequestration of said substrate, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.
139. (New) A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell with a substrate exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide encoded the nucleic acid molecule having the sequence of SEQ ID No: 1;
- (b) contacting said cell with a candidate modulator of MRP- β ;
- (c) assaying for a detectable fluctuation in export or sequestration of said substrate, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

140. (New) A method of identifying a modulator of MRP- β , comprising the steps of:

- D/11
- (a) contacting a cell with a substrate exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide by the DNA insert of the plasmid deposited as ATCC Deposit No. 94809;
 - (b) contacting said cell with a candidate modulator of MRP- β ;
 - (c) assaying for a detectable fluctuation in export or sequestration of said substrate, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

141. (New) A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell with a cytotoxin exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide encoded by a nucleic acid molecule which hybridizes under conditions of hybridization in 0.5M NaHPO₄ at 65°C followed by washing in 0.1xSSC at 68°C to a complement of the nucleic acid molecule having the sequence of SEQ ID No: 1;
- (b) contacting said cell with a candidate modulator of MRP- β ;
- (c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

142. (New) A method of identifying a modulator of MRP- β , comprising the steps of:



- D11
- (a) contacting a cell with a cytotoxin exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide encoded the nucleic acid molecule having the sequence of SEQ ID No: 1;
 - (b) contacting said cell with a candidate modulator of MRP- β ;
 - (c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.

143. (New) A method of identifying a modulator of MRP- β , comprising the steps of:

- (a) contacting a cell with a cytotoxin exported or sequestered by MRP- β , said cell expressing a vector-derived MRP- β polypeptide by the DNA insert of the plasmid deposited as ATCC Deposit No. 94809;
 - (b) contacting said cell with a candidate modulator of MRP- β ;
 - (c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP- β modulator.
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